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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,633	11/08/2000	Stephen B.H. Kent	TSRI 478.0C1	6210

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/21/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

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Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/710,633	Applicant(s) KENT ET AL.	
	Examin r Jeffrey E. Russel	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2000 and 06 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons:

The Sequence Listing filed August 6, 2001 was not accompanied by a statement that the sequence listing includes no new matter, as required by 37 CFR 1.821(g).

The Sequence Listing filed August 6, 2001 was not accompanied by amendment instructions requesting that the paper copy of the sequence listing be inserted into the specification and requesting that the originally-filed paper copy of the sequence listing be deleted from the specification.

SEQ ID NOS need to be inserted after each amino acid sequence recited in the specification, e.g., at page 12, lines 13, 19, and 20, and page 29, line 12. See 37 CFR 1.821(d). When the Schemes (e.g., Schemes 3 and 4) set forth in the specification are re-submitted as drawings (see paragraph 2 below), then either the drawings or the Brief Description of the Drawings will need to be written so as to include the appropriate SEQ ID NOS.

Correction is required.

The computer readable form the sequence listing filed August 6, 2001 was approved by STIC for matters of form.

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an

earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). The claim for priority should also include a statement that parent application 08/710,653 is a national stage application filed under 35 U.S.C. 371 based upon PCT/US95/05668, filed May 4, 1995.

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

4. The disclosure is objected to because of the following informalities: The "Government Rights" paragraph should be the second paragraph of the specification, following immediately after the priority claim. See MPEP 310. The Schemes set forth in the specification constitute flowcharts and/or figures, and need to be deleted from the specification and re-submitted as proposed new drawings. See 37 CFR 1.58(a). A Brief Description of the Figures will then have to be inserted into the specification as required by 37 CFR 1.74, and references in the specification to "Scheme 1", etc. will have to be amended to read "Figure 1", etc. At page 9, line 24, one of the two occurrences of "the" should be deleted. Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 10-16, 20-24, and 26-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 8 and 24 recite generically the reaction of a second oligopeptide having an N-terminal amino acid residue having an unoxidized sulfhydryl side chain and a free amino group that is capable of forming a β-aminothioester linkage with a C-terminal thioester. The N-terminal amino acid residue is not required to be a cysteine residue (compare dependent claim 9). However, the original disclosure of the invention is limited to second oligopeptides in which the N-terminal amino acid residue is a cysteine residue (see, e.g., page 1, lines 6-7; page 14, lines 21-23; and page 29, lines 25-26). The disclosure of a species, i.e. a cysteine residue, does not provide written descriptive support for the more generically claimed N-terminal amino acid of claims 8 and 24. For analogous reasons, there is no original disclosure of a third oligopeptide having an N-terminal amino acid residue having an unoxidized sulfhydryl side chain and a free amino group that is capable of forming a β-aminothioester linkage with a C-terminal thioester. There is no original disclosure of derivatives of naturally isolatable proteins containing one or more cysteine residues that are not found in the naturally isolatable protein (see claims 11, 20, and 28). The original disclosure does not include the concept of altering a naturally-occurring protein's amino acid sequence by replacing amino acids with cysteine residues or by inserting cysteine residues into the amino acid sequence so that a derivative of the naturally-occurring protein can be synthesized by the disclosed method. There is no original disclosure of the method steps of claim 15 in which the second oligopeptide also has a C-terminal thioacid which is converted into a thioester and then become the first oligopeptide for purposes of a

second sequential native chemical ligation. Sequential native chemical ligations are not disclosed in the specification, nor is a second oligopeptide having the structure required by instant claim 15. Applicants have not indicated where the new claim limitations are supported by the original disclosure of the invention.

6. Claims 8-16, 19-23, and 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. At claim 8, lines 14 and 15, and claim 15, lines 13 and 14, "fragment" (each occurrence) should be deleted so that the claim terminology is consistent with that used at claim 8, lines 3 and 6, and at claim 15, lines 2 and 5-6. Note that while the oligopeptides are fragments of the desired protein or domain thereof, fragments of the oligopeptides are not used in the claimed method. There is no antecedent basis in the claims for the phrase "said desired protein" in claims 19, 20, 27, and 28. Note that independent claims 17 and 24 does not use the terminology "desired".

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8-14 and 17-31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,184,344. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '344 patent anticipate instant claims 8 and 9. With respect to instant claims 10-14, while the '344 patent does not claim the synthesis of naturally isolatable proteins such as human cytokines, it would have been obvious to one of ordinary skill in the art to use the claimed synthesis method of the '344 patent to synthesize any oligopeptide, including naturally isolatable proteins including human cytokines, because these are known proteins for which it is desirable to synthesize for therapeutic use, and because the claimed synthesis method of the '344 patent would have been expected to be useful in the synthesis of any such proteins which comprise cysteine residues. With respect to instant claims 17-31, a method of making a product suggests the product made.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 8-10, 12-14, 17-19, 21-27, and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 96/34878 (which issued based upon Applicants' priority document PCT/US95/05668). The WO Patent Application '878 teaches Applicants' claimed

invention. This rejection will be withdrawn once Applicants have inserted the appropriate claim for priority into the specification (see paragraph 2 above).

10. Claims 8-10, 12-14, 17-19, 21-27, and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by the Dawson et al article. The Dawson et al article teaches ligating two oligopeptides, one oligopeptide having a C-terminal thioester and the other oligopeptide having an N-terminal cysteine residue, in the presence of a thiol. Spontaneous rearrangement results in the formation of an amide bond. The oligopeptides are prepared by solid phase synthesis and conversion of the C-terminal thiol. See, e.g., page 777, column 1 and Figure 1, and page 778, footnote 2. This rejection will be withdrawn once Applicants have inserted the appropriate claim for priority into the specification (see paragraph 2 above).

11. Claims 17-20 and 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by the Abrahmsen et al article. The Abrahmsen et al article teaches a subtilisin derivative in which the Ser221 residue is converted to a Cys residue. Subtilisin is a bacterial serine protease. See, e.g., the Abstract and page 4151, column 2, lines 7-8. Note that process of making limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art.

12. Claims 17-19, 21-27, and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by the Clark-Lewis et al article (Biochemistry, Vol. 30, pages 3128-3135). The Clark-Lewis et al article teaches synthetic human IL-8. See, e.g., the Abstract. Note that process of making

limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art.

13. Claims 17-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Bell et al. Bell et al teach synthetic human interferons in which tyrosine residues are replaced with cysteine residues. See, e.g., the Abstract and claim 1. Note that process of making limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art.

14. Claims 17-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Shaw et al. Shaw et al teach human IL-3 in which a cysteine residue is either inserted into the N-terminal region or else is substituted for an amino acid in the region. See, e.g., the Abstract and claim 1. Note that process of making limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 305-7401 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1653

JRussel
December 20, 2001